

A)

	Motif 1	Motif 2	Motif 3	Motif 4
Rv2837c_Mt	VGWVCHVEDADTIGAGLALALVLDGCG [35]	VDLVTVVDIPSDRLGALG [6]	RELVVIDHHSND [10]	SADSTTWAEILDANGKPIDPRVAHCYAGIADTGSFRWASV
sl11253_Ssp	DLILCHQTADFDVILGRAVGLAKLHPSGR [34]	IRSLYIVDQGGDLRGKAA [8]	RQVAIYDHHNSP [11]	AVGASTTLIVEKLQRADISLSNVERSVMALGIHVDTGSLTFTQT
MCPA_Mg	IVIFHHVREDGDCIGAQGLFHLIKANF [32]	EALAIWVDANYKNRIELRE [7]	KAVLRIDHHPNED [11]	SYVACCEQIVEMATVAKWTIPPVAATLLYIGIYDPSNRFLYSNT
YTI_Bs	IILHRHVREDPDAYGSCGLTEILRETY [30]	GALVIVQDTANQERIDDR [4]	AKLMKIDHHPNED [13]	SVSEMIYELYEGKEHGKLNKAAELIYAGIVGTGRFLFPNT
AF2029_Af	LGIFTHDNEFDPSMSSAYALREIAKQFD [37]	YDAFAIVDSSGPGVNSIP [3]	DISIVIDHHPAEK [10]	DVGATATILTEYIKELKITPSKILATALFFGIKSEDEFKRNTR
MJ0977_Mj	NKILIVTHIDTGLTSRAILQKLAERLN [23]	YDLITFADLGSGQLMWKE [11]	DKIITIDHHQPEE [18]	GAEICGAGVSYLEFAKAINNDWIDLAKYAVILGAVGDIQNIIEGKLI
MJ1198_Mj	RPIIIRHHPDIDGYCGGIALEKAILPII [46]	LPLIVLDNGSTDEDIPAI [7]	IEVIVIDHHFEGE [85]	KGRTYDREYLEKIALCNDFEAFYLRFMDEKGIIVDPILATNIKEF
HP1042_Hp	MQVYHLSHIDLDGYACQLVSKQFFKNIQ [27]	EFLIVSDNLNLNNEAREYL [13]	IQIQLIDHHISGK [19]	IVYEFLKKHYAILEPKNTTWLEPLVENVNSVDIWTQGYGFELG
RecJ_Hi	QKIVIVGDFDADATSTALSVALRQLG [31]	VQLIATVDNGVSSFDGVAF [5]	IRVLVTDHLLPPE [33]	LAVRAKFERELGIFTAETQPNFTDLDLVALGTIADVVPLDQNNR
RecJ_Hp	TEILVVGDDYDADGVISSAINAKFFESLN [27]	APLIITVDNGINAFERARF [5]	YTLIITDHHCLHH [27]	LNAFYLCYGIHQILGKEKSHSELCLAGVATIANMPLTFFNR
RecJ_Ssp	EKVTIWGDFDADGITSTAVLWEGLGQFF [32]	TKLIIVTQDTGSTNLDEIVY [5]	MDVIVTDHHTLPD [27]	VAFKLVEALYNQYPTVPQOPLEDLIDLVAIGLIADLVLTQGDOR
YYBQ_Bs	ILIFGHQNPDTITCSAIAYADLKNKLG [36]	VNGVILVDHNERQQSIKDI [3]	QVLEVIDHHRIAN [12]	PVGCTATILNKMYKENNVKIEIAGMLSAIISDLSLFKSPTC
ICRA_Sg	ILVFQHQNEPDAIGSSYAFAYLAREAY [38]	AEQVILTDHNEFQQSVADI [3]	EVYGVWDHHRVAN [12]	PVGSASSIVYRMFKESVAVSKEIAGMLSGLSIDTLLKSPYT
Y608_Mj	RYVVGHKNPDTDSIASAIVLAYFLDCYP [31]	GKEIILVDHSEKSSQSFDDL [3]	KLIAITDHHKUGL [19]	IAELYFKDAIDLIGGKKKELKPDLAGLLLSAISDITVLFKSPTT
AF0756_Af	VYVVGHKNPDTDSVCSAIFAYLWKNWK [46]	GKKVALVDHSEKAQTVDGI [3]	EWVAIVDHHKIGD [12]	PVGCTATVIKLLFDKGTGVEIPKDIAGILLSILSDITVIFKSATT
U60409_Lm	TVVQNEGQDSDSIVGCIYLANLFDKQP [44]	QIAHNLDIAALNASWLY [14]	RVVGWVDHHEDEQ [11]	LRTVGSACTLVTELYREGGEDVVCPTLLTAPIVLDITVNFEPQAK
PPX1_Sc	TICVGNESADPDSIASAITYSYCYIYN [62]	ELNSYLVNDNDTPKNLKNY [2]	NVVGILIDHHFDLQ [14]	SCSSLVFNWYWEKLGQDREVWNIAPLIMGAILIDTSNMRRKVE
PRUNE_Dm	HLVMGNESQDLSAVSAVTLAFVYAQRH [48]	DVNVLVDHHSVPLAPNVT [1]	NVTEIIDHHRPLED [18]	SVGSCATLVAQRYLAEDQPRSTVAQLLHATIVLDITINFAPAAK
h-prune.1_Hs	HWVLGNEACQDSTVSALALAFYLAKT [52]	QTLTILVDHHLISKSDTAL [2]	AAVEVIDHHRPIEP [12]	LVGSCATLVTERILQGAPEILDRTAALLHGTIILDVNMWDLKIG

specific motifs

	Gis
Rv2837c_Mt	[107] TVNLAAVASGFGGGGHRLLAAGYTTGS 1648883
sl11253_Ssp	[123] DTDLTQLLEFPYGGGGHAQAAAVNLRDV 1653244
MCPA_Mg	[102] GINVRDIAIKYGGGGHNNVASCALITNK 1045875
YTI_Bs	[103] GPVINGLARKYNGGGHPLASCASIYSW 2293259
AF2029_Af	[102] EVLRRAFQDVGSAAGHAHAAGAIPLG 2648507
MJ0977_Mj	[254] AIKYASEKVNCGGGGHKFAAGAYIPDN 2128614
MJ1198_Mj	[109] QLMEEIPEASLDGGGHECAGSLKFVEG 2128720
HP1042_Hp	[137] CDVCELSQMCNCGGGHNRVASCCKIDGF 2314198
RecJ_Hi	[168] RIHSQHNNILKFGGHAMAAGLSIREE 1172895
RecJ_Hp	[155] DALNGVSSLLJGVGGRQACGLSVEKN 2313437
RecJ_Ssp	[165] ALLHSQRHMLGFGGHPFAAGLSLPLD 1652638

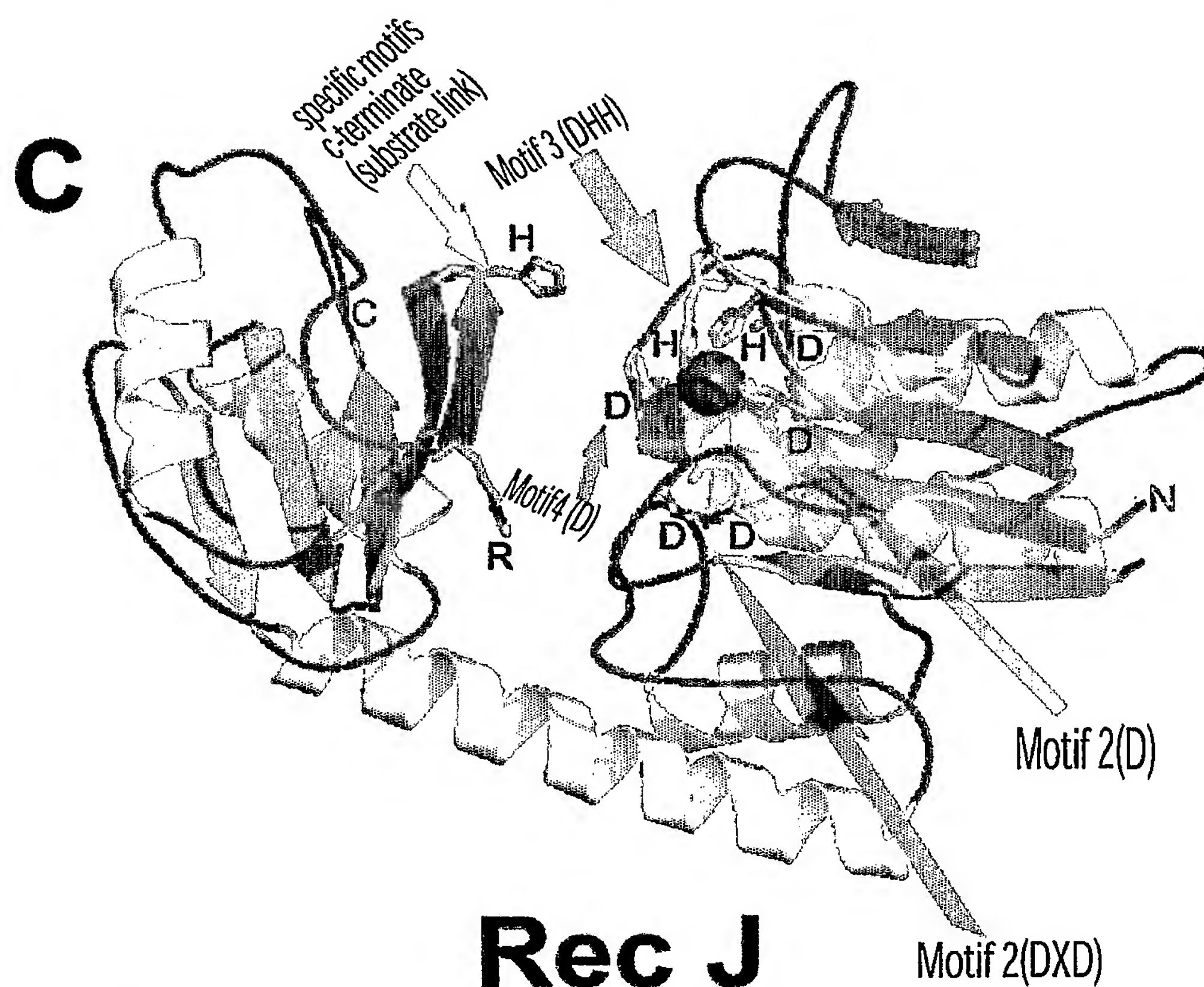
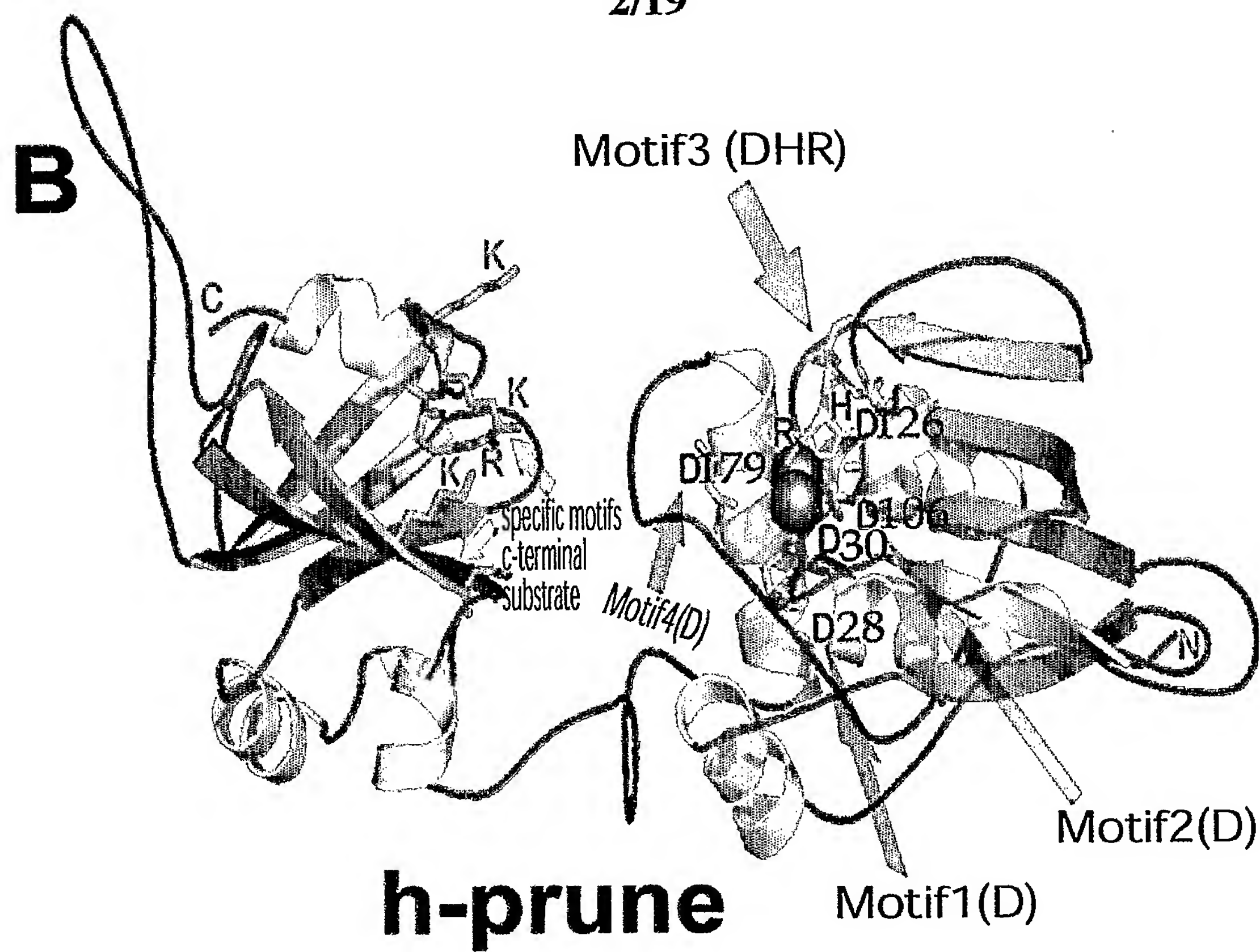
Family 1

YYBQ_Bs	[31] DLSKKTVEELSLDAKEFTLG [75]	TALLKGVNSRKKQVWFVLT	586817
ICRA_Sg	[31] NLASKSAEELIDDAKTFFELN [75]	HAFLAGAVSRKKQVWFQLTE	1743856
MJ0608_Mj	[32] VVGKLPKEEINMDFNFDEN [74]	SVFLEGVMSRKKQVWFPEER	1591318
AF0756_Af	[32] AVDDLTAMDITKRDYKDEMS [75]	SWWLDGVMRKKQVWFPEEK	11498362
L2759.9_Lm	[36] DVLALSVPQILRRDYKQFSFK [105]	YSLSDPSISRKK-LVPAIASE	1407725
PPX1_Sc	[41] DIKGFVSVDILKDYKQNFQ [97]	MEKQLNVEATRKKQVWFPEE	730369
PRUNE_Dm	[37] DISKLTLEVLKDKMKVLQFD [97]	LRQHNVAQRKH-ILPIVKR	1079081
h-prune.1_Hs	[34] DVSGLTTEQMLRKDKQKTYRQ [94]	YLGQNTQVSRKK-LIPLAQE	11245938

Family 2

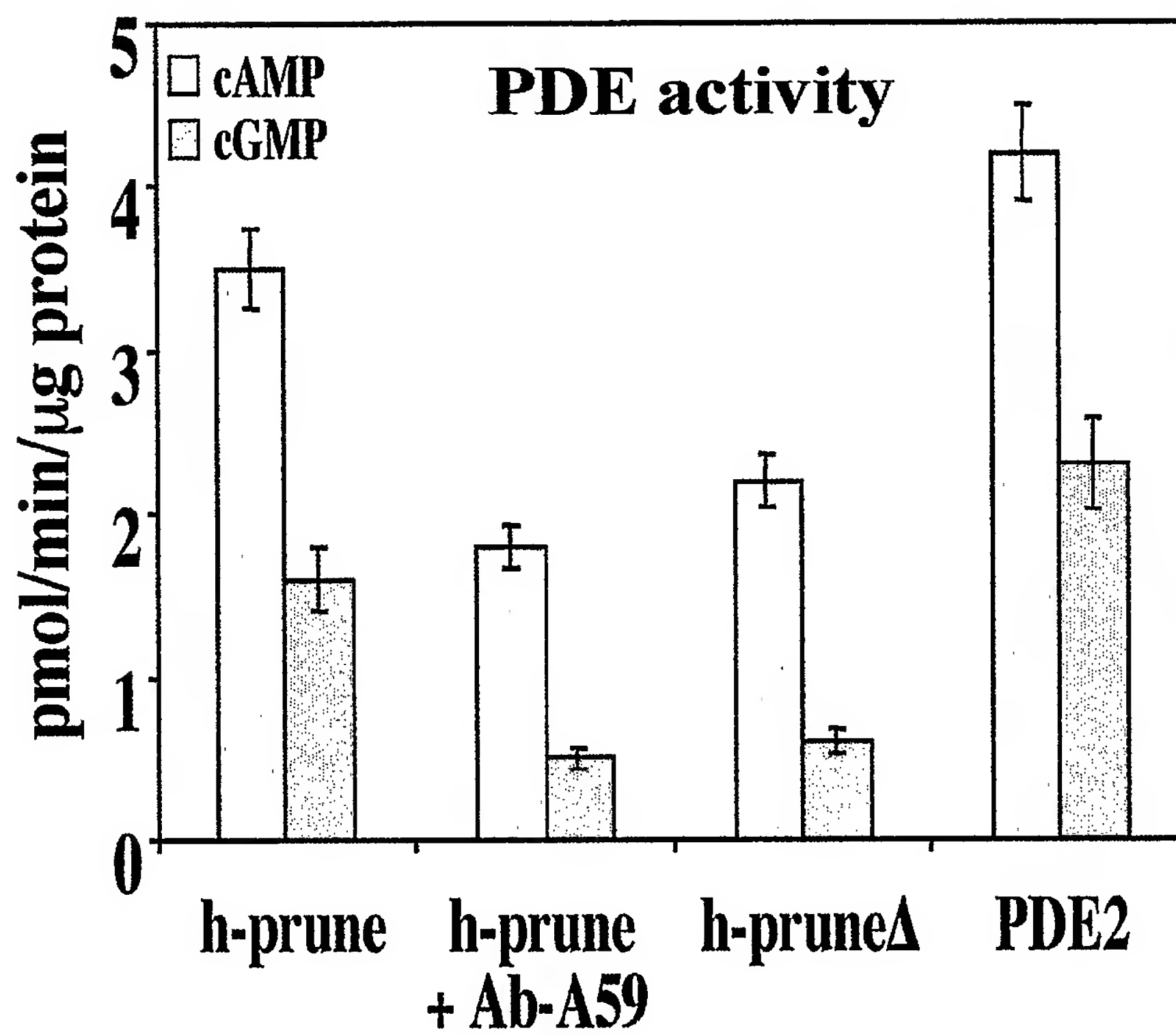
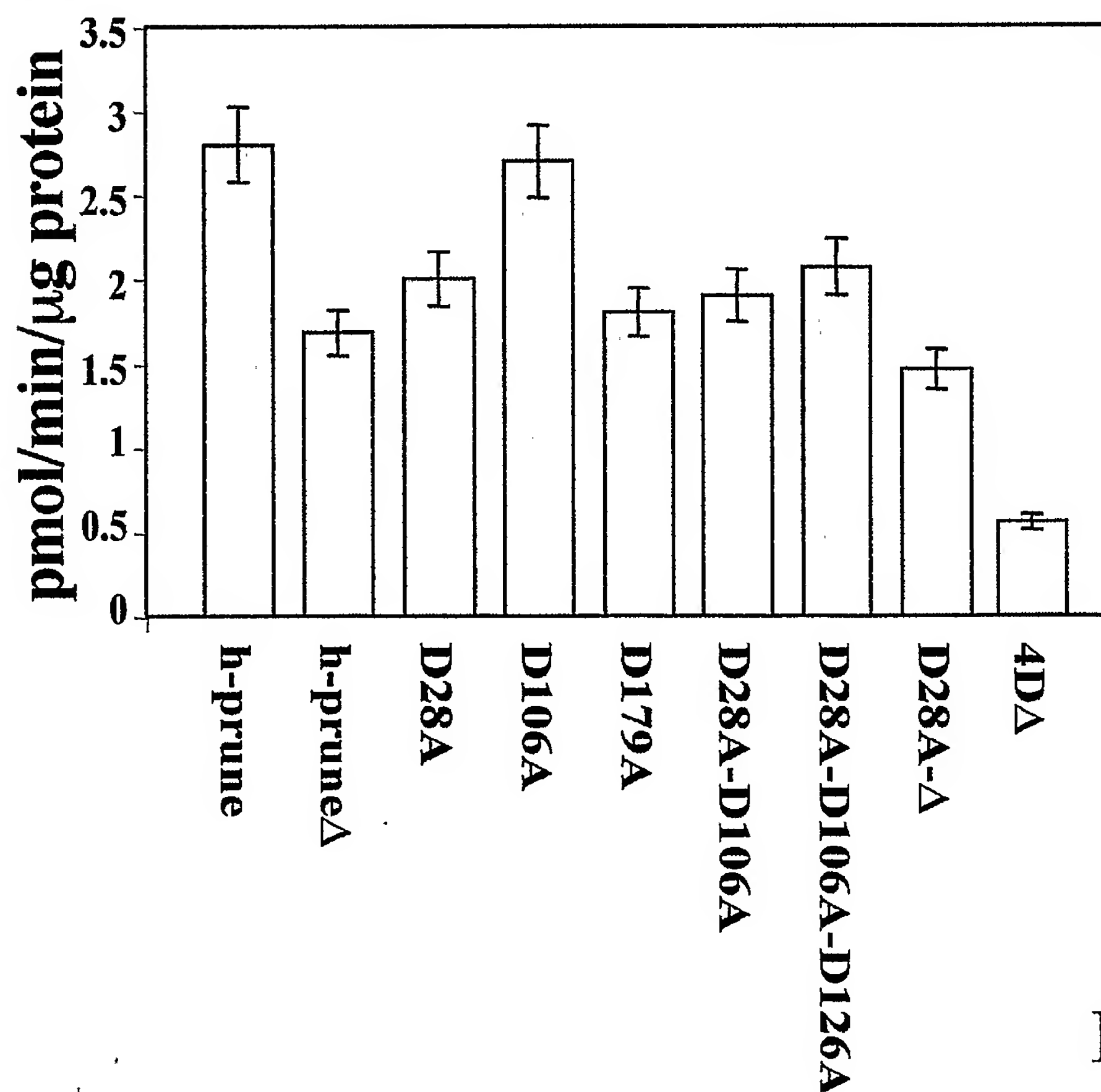
Fig. 1

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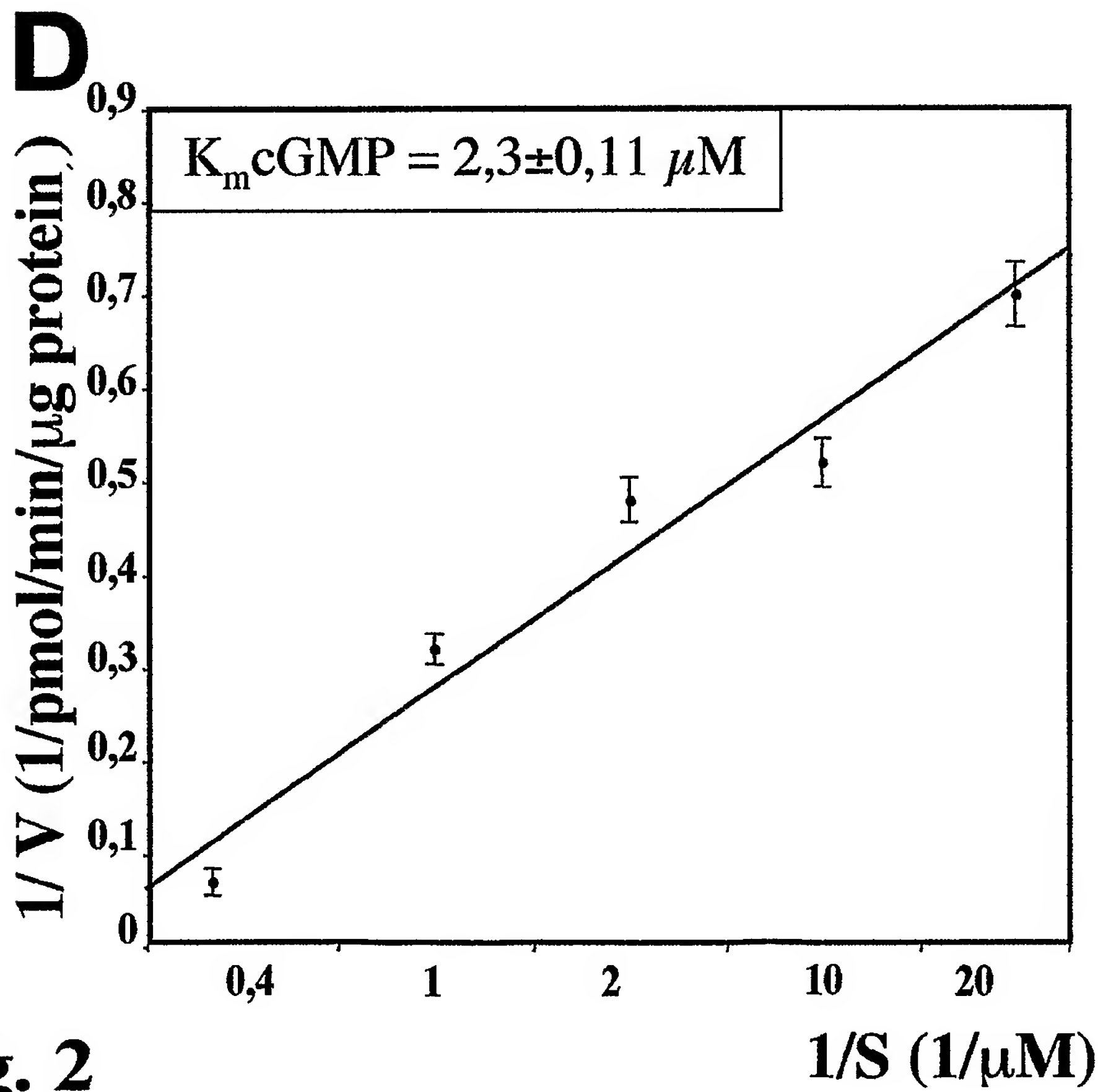
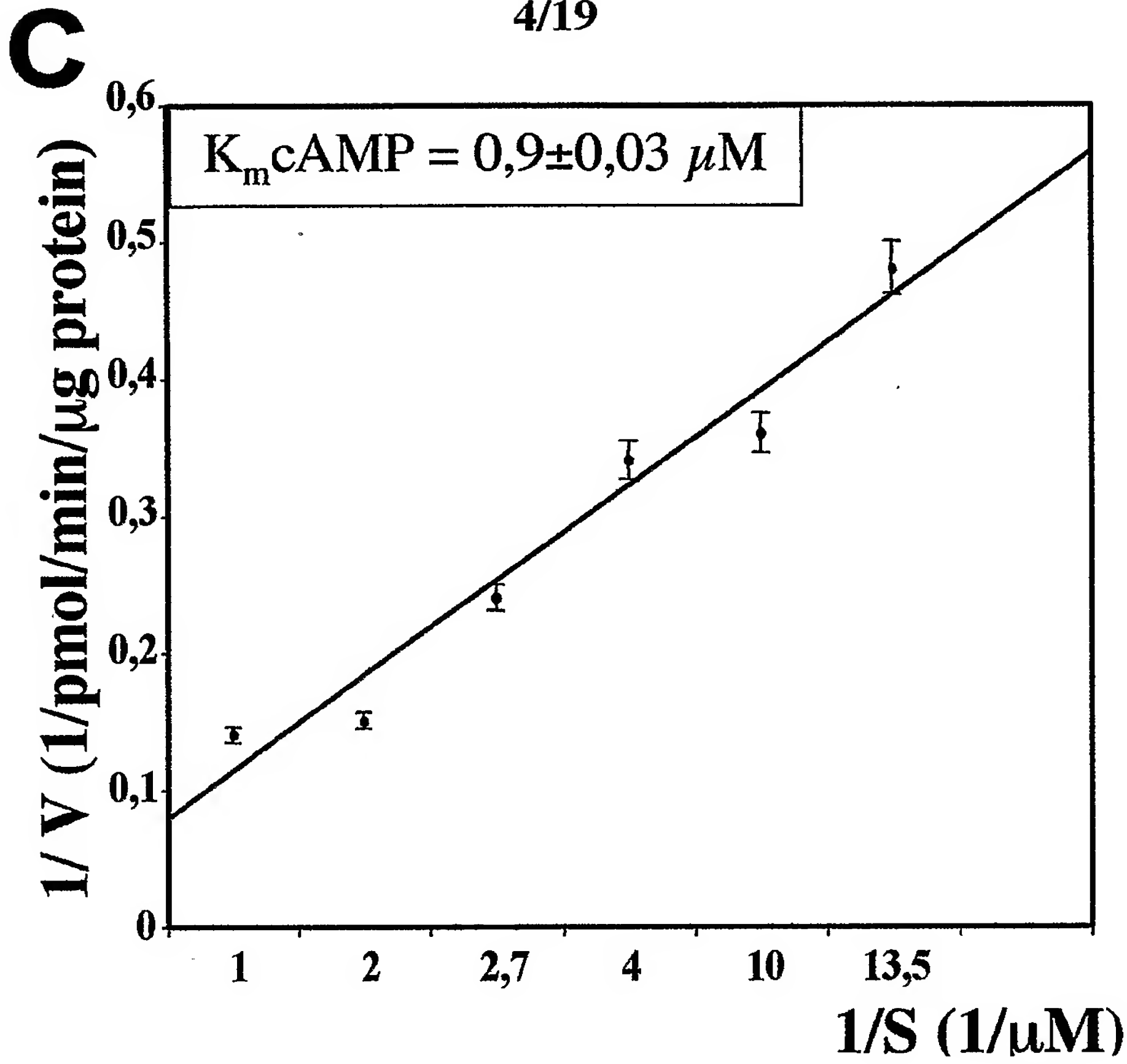
**Fig. 1**

**A**

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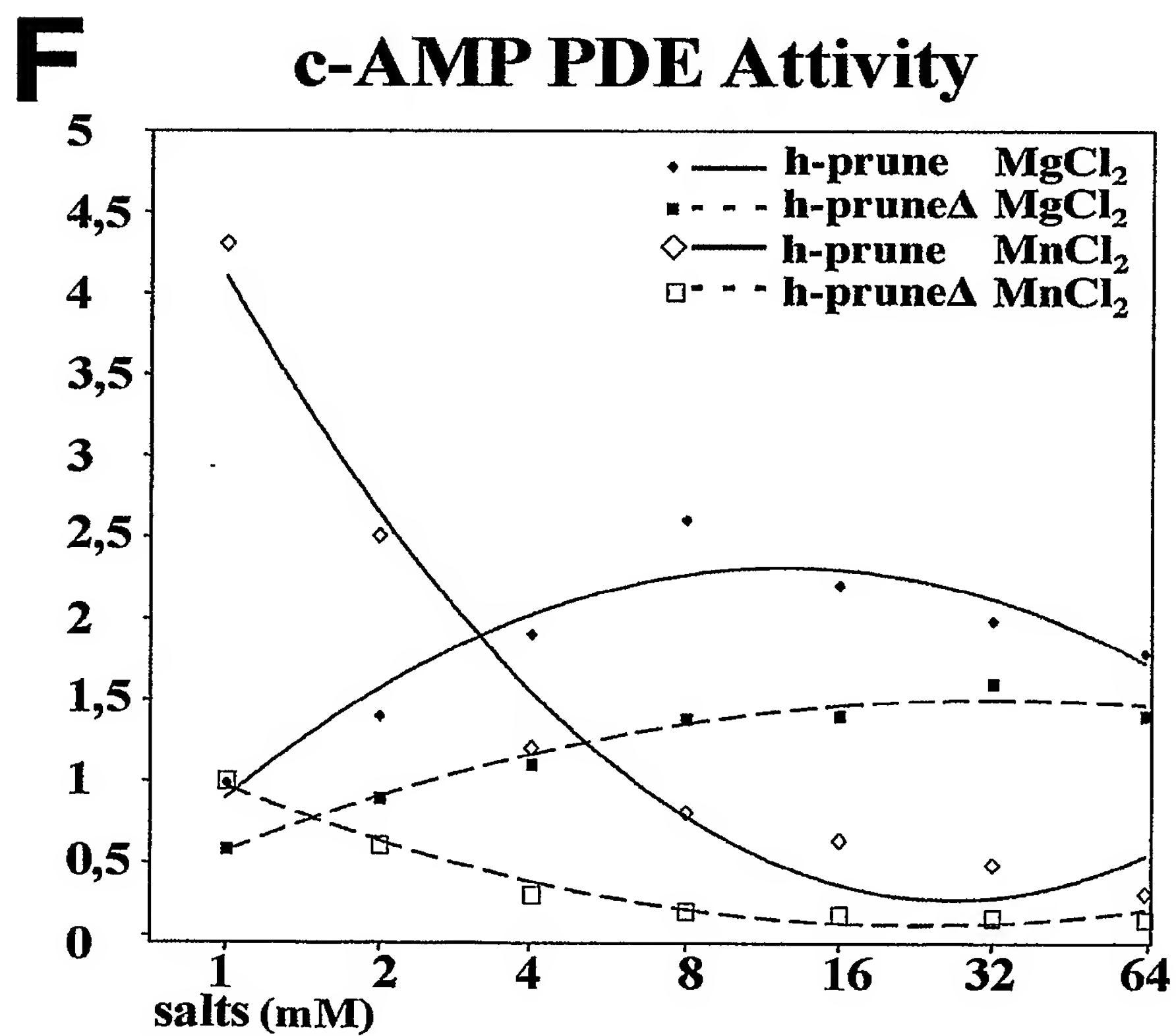
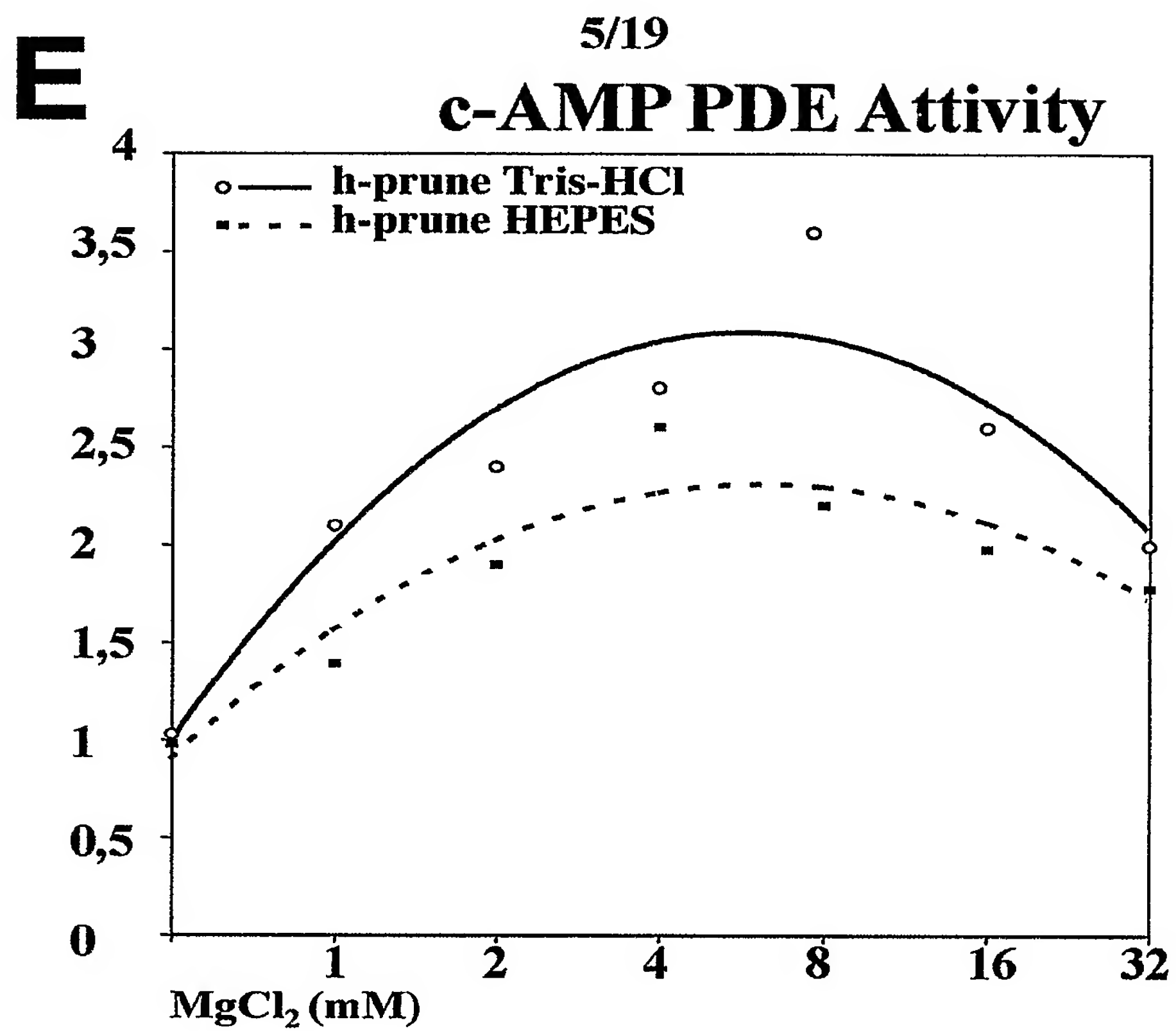
**B****Fig. 2**

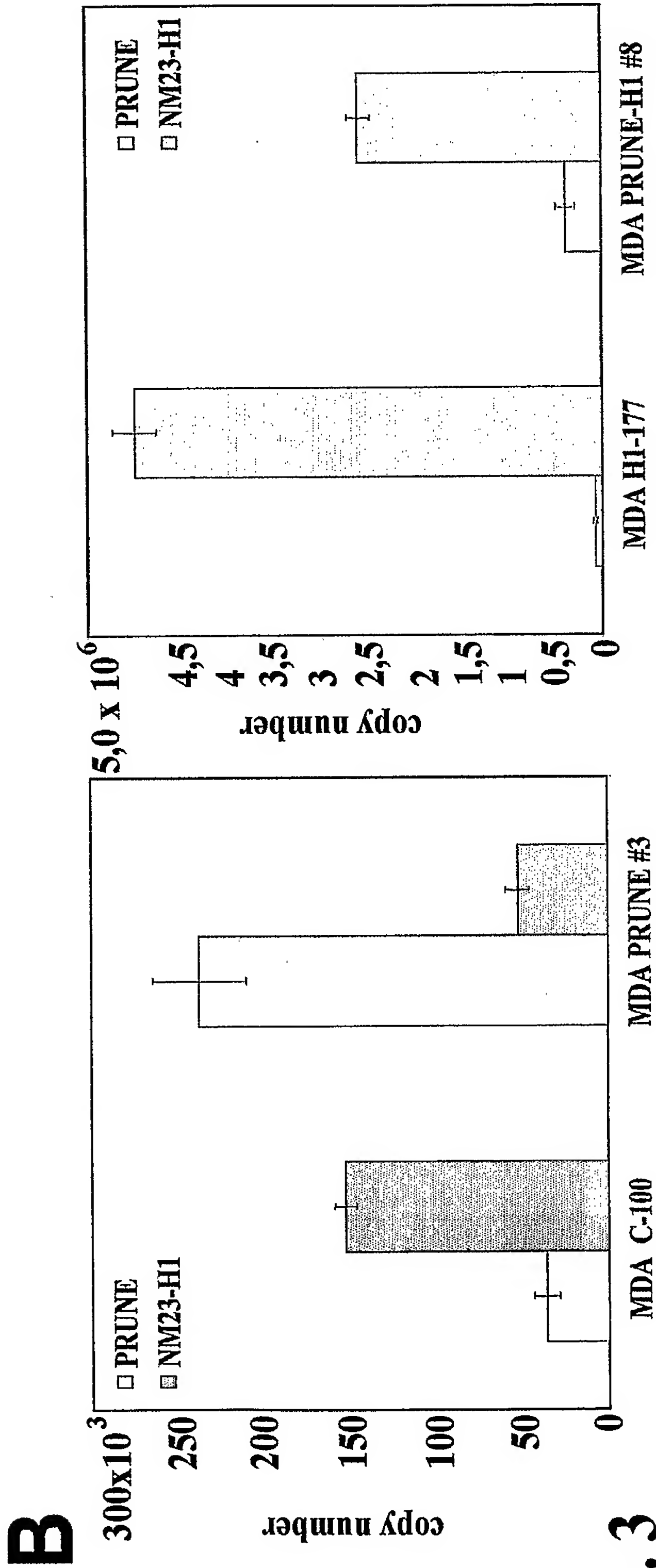
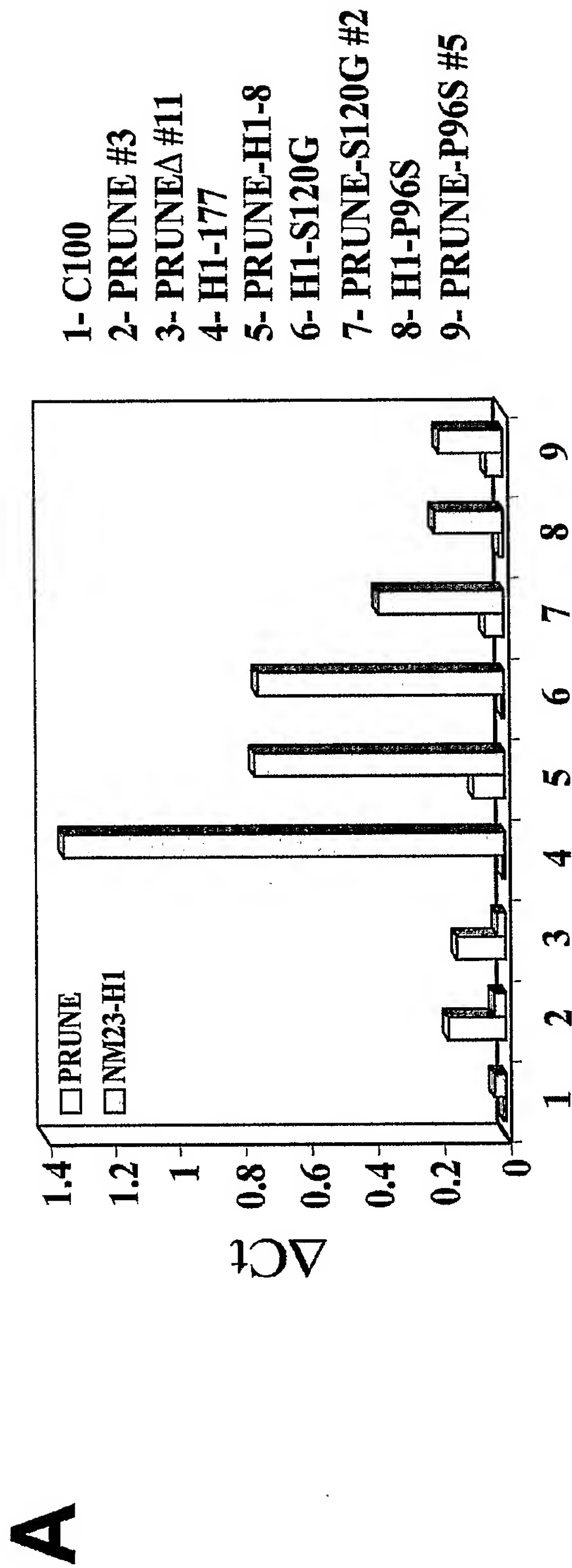
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**Fig. 2**



**Fig. 2**



**Fig. 3**

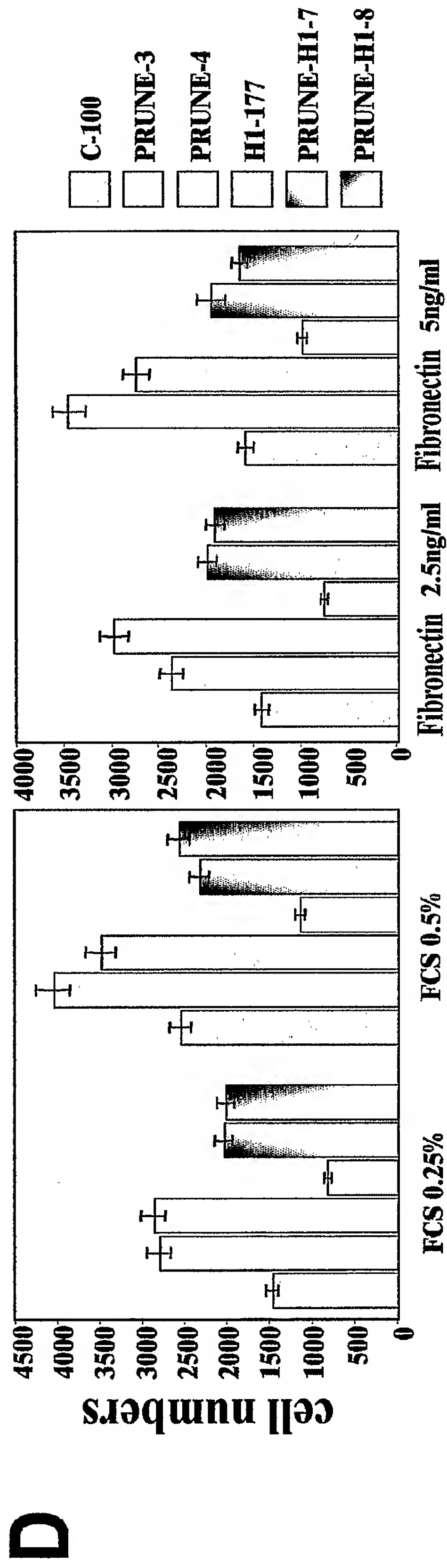
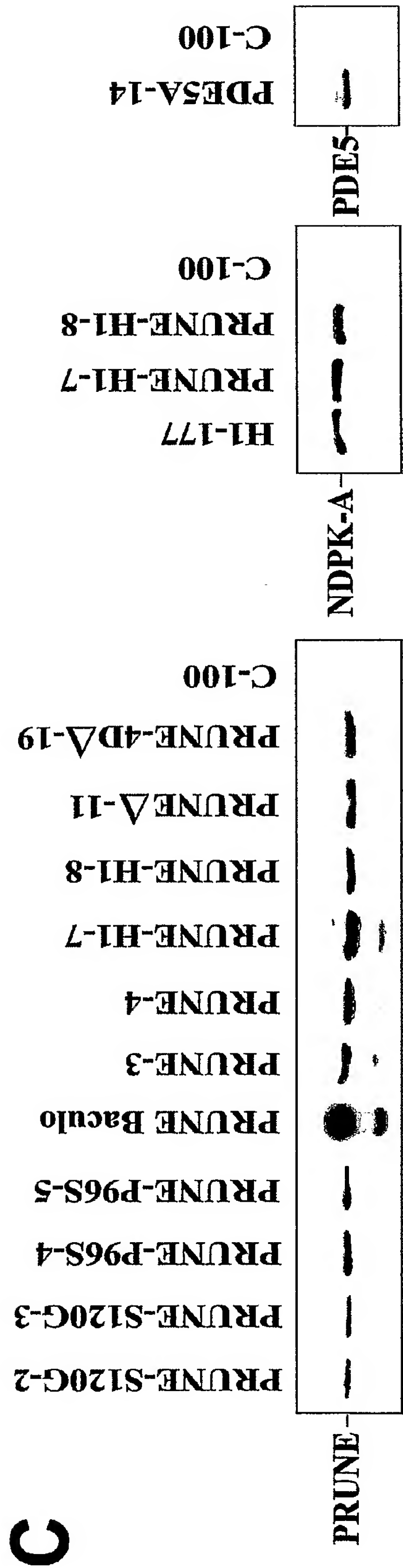
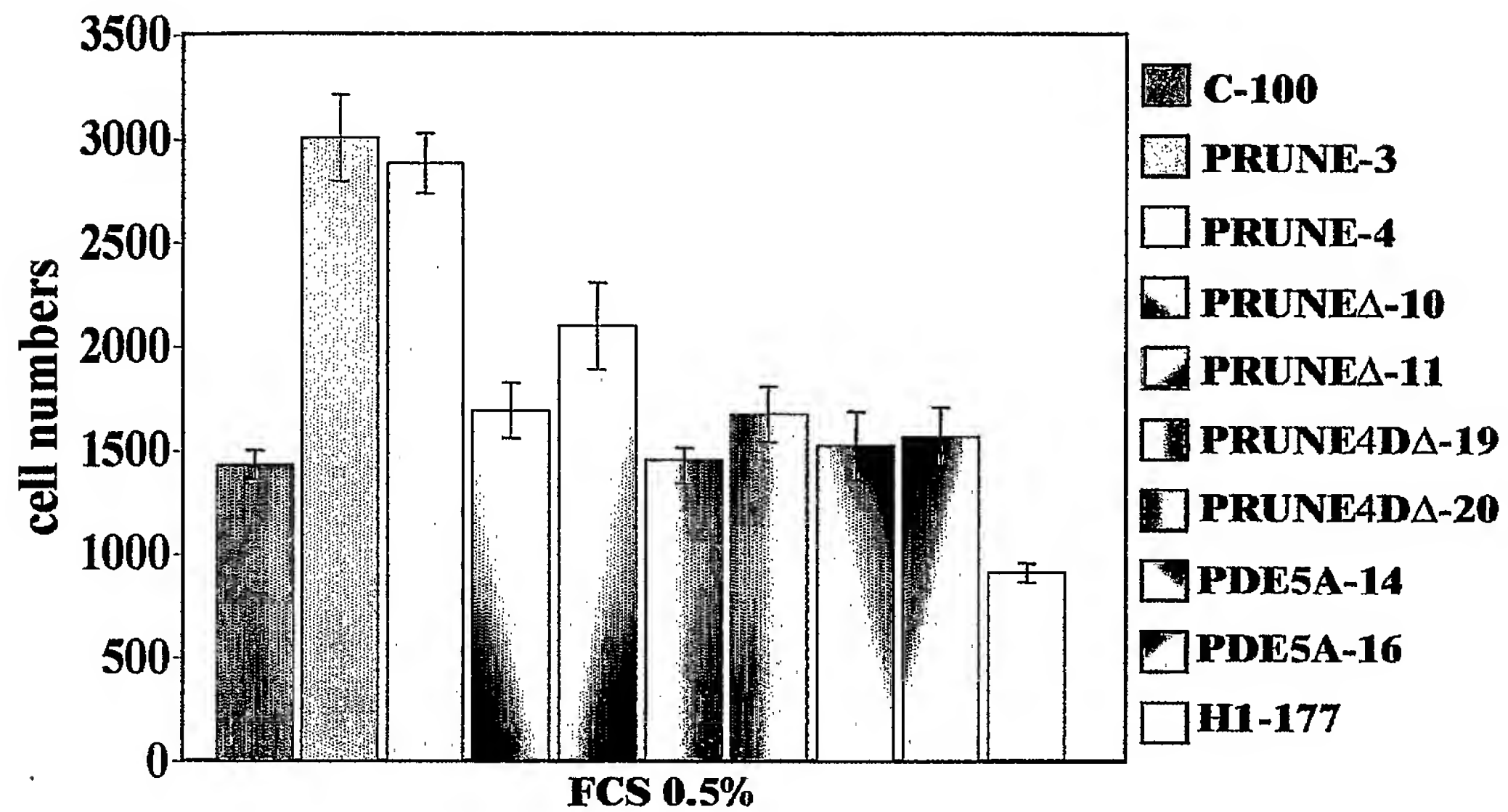
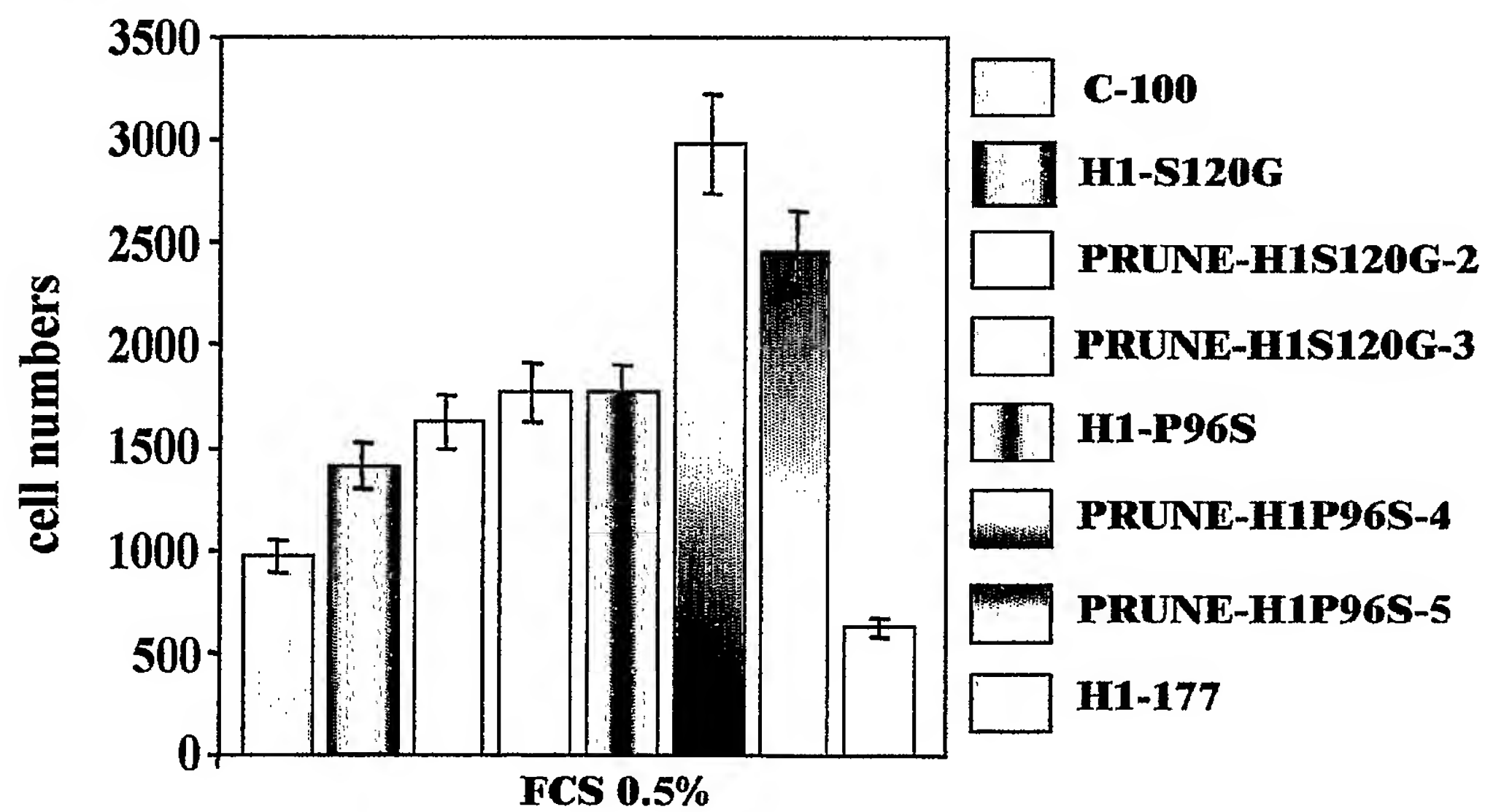


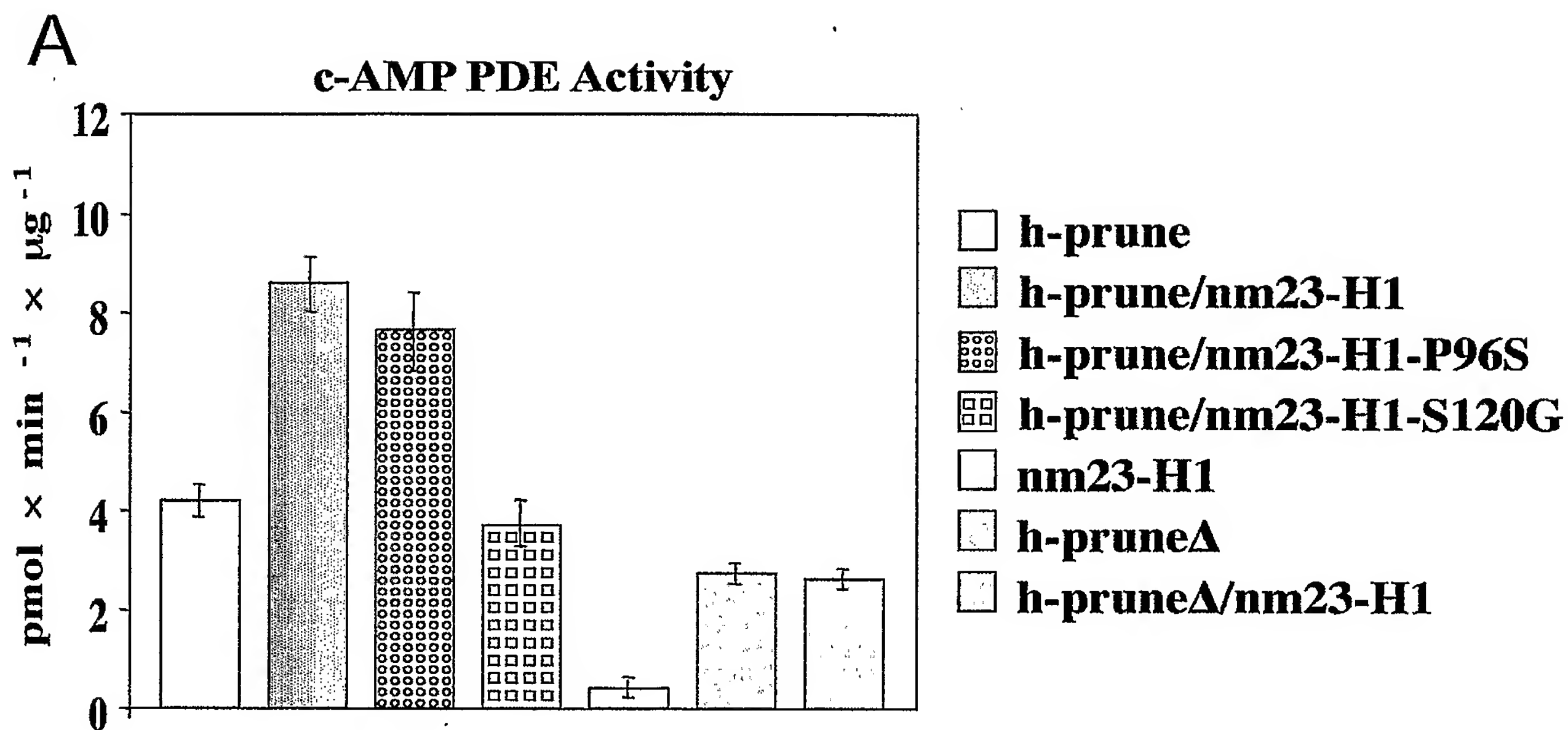
Fig. 3

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**E****F****Fig. 3**



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**B**

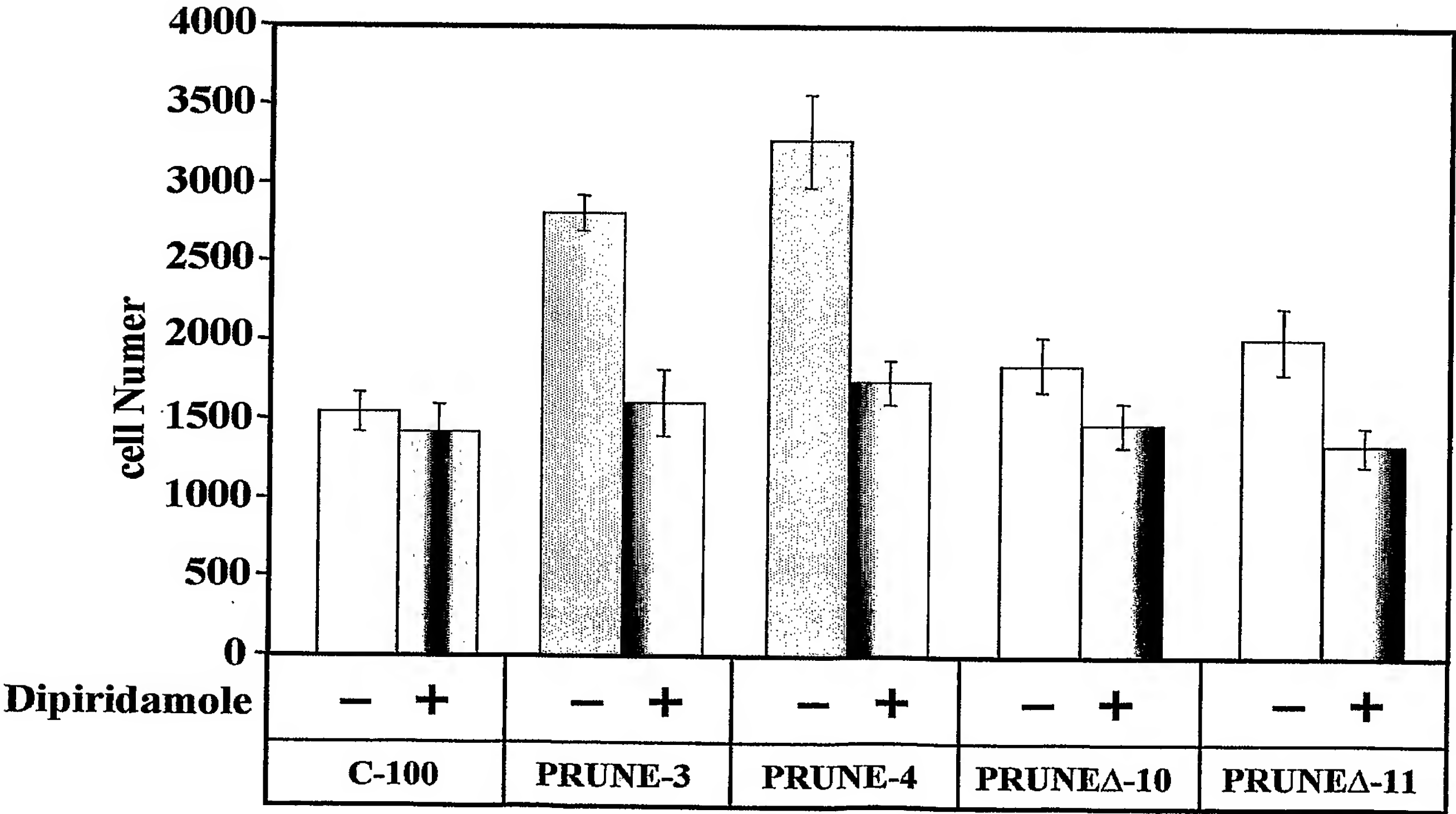
lone name	PDE h-prune Activity (pmol $\times$ min <sup>-1</sup> $\times$ $\mu$ g <sup>-1</sup> )	Motility cell number
MDA C-100	3.8 $\pm$ 0.7	1548 $\pm$ 84
MDA H1-177	2.2 $\pm$ 0.4	928 $\pm$ 73
MDA PRUNE #3	35 $\pm$ 5.3	2812 $\pm$ 294
MDA PRUNE #4	28.7 $\pm$ 2.5	3272 $\pm$ 271
MDA PRUNE $\Delta$ #10	16.8 $\pm$ 1.2	1682 $\pm$ 64
MDA PRUNE $\Delta$ #11	14.6 $\pm$ 0.9	2087 $\pm$ 97
MDA PRUNE-H1 #7	18.8 $\pm$ 2.6	2048 $\pm$ 93
MDA PRUNE-H1 #8	22 $\pm$ 4.2	2006 $\pm$ 87
MDA H1S120G	2.4 $\pm$ 0.8	1328 $\pm$ 54
MDA PRUNE-H1S120G #2	4.4 $\pm$ 1.6	1624 $\pm$ 89
MDA PRUNE-H1S120G #3	5.3 $\pm$ 1.4	1767 $\pm$ 108
MDA H1P96S	3.0 $\pm$ 0.3	1742 $\pm$ 38
MDA PRUNE-H1P96S #4	19.2 $\pm$ 0.3	2982 $\pm$ 184
MDA PRUNE-H1P96S #5	11.6 $\pm$ 0.4	2448 $\pm$ 143

**Fig. 4**

**A**

Inibitor	Selective for a PDE type	IC <sub>50</sub> μM	h-prune IC <sub>50</sub> μM
Cilostamide	PDE3	0.05	>100
Dipiridamole	PDE5/6/9/10/11	0.9/0.38/4.5/1.1/0.37	0.78±0.05
IBMX	non selettivo	2-59	40.2±0.8
Milrinone	PDE3	1.3	>100
Rolipram	PDE4	2.0	>100
Vinpocetine	PDE1C	8.1	22.3±1.1
Zaprinast	PDE1/5/6	6.9/0.76/0.15	>100
Sulindac	cGMP PDEs	—	>100

**B**



**Fig. 5**



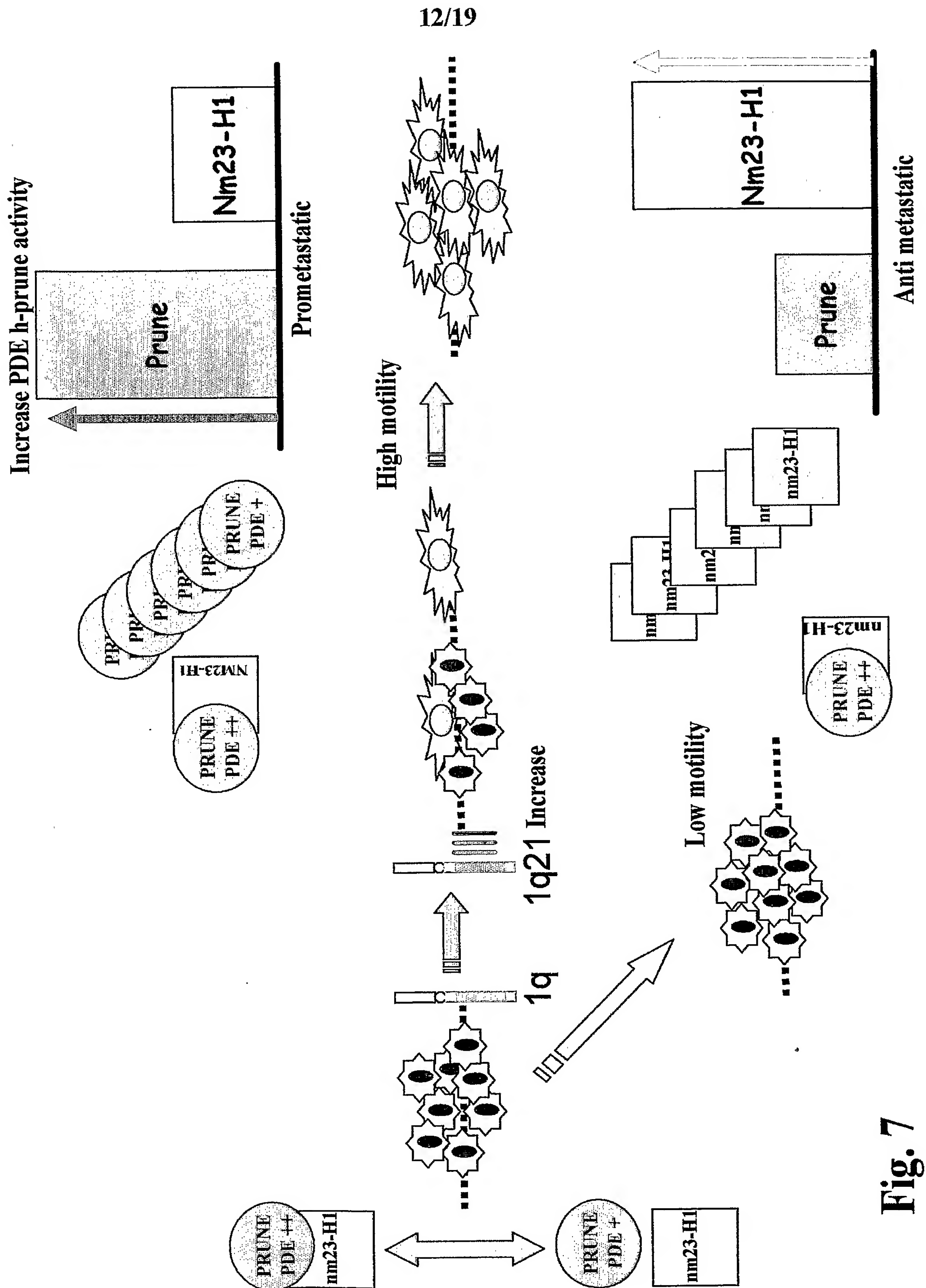
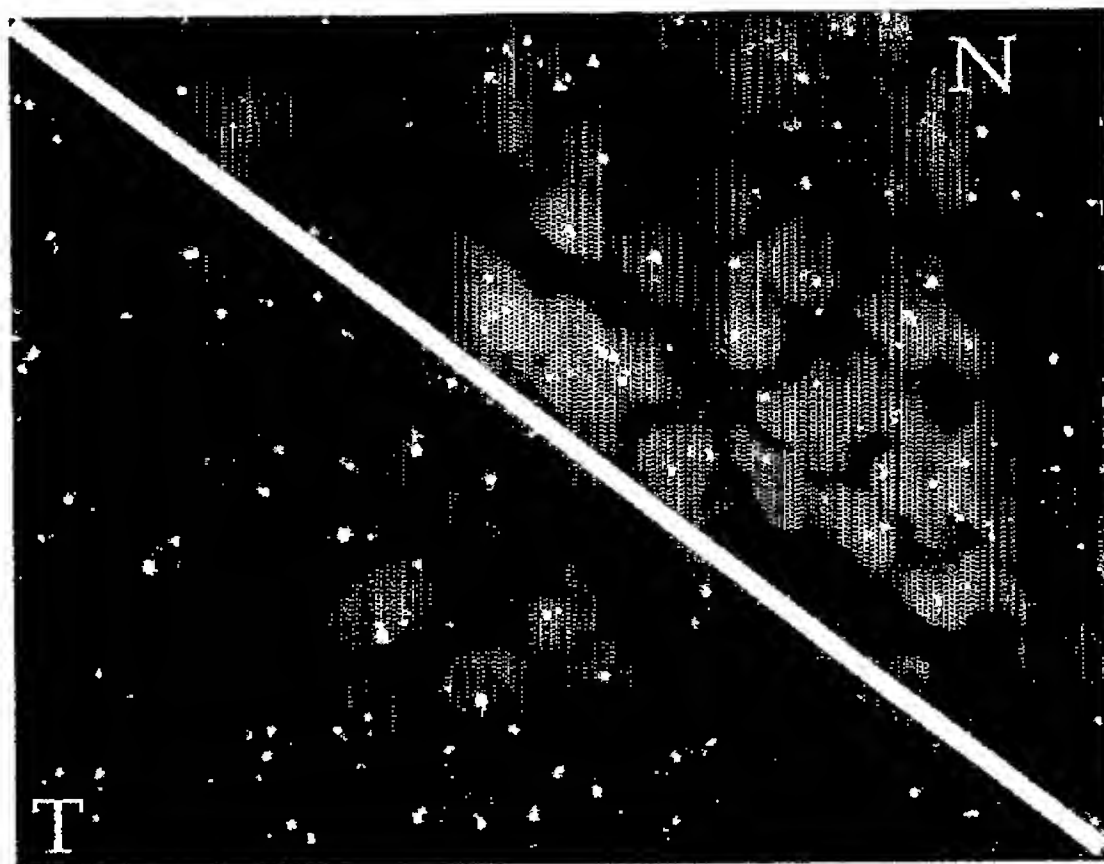


Fig. 7

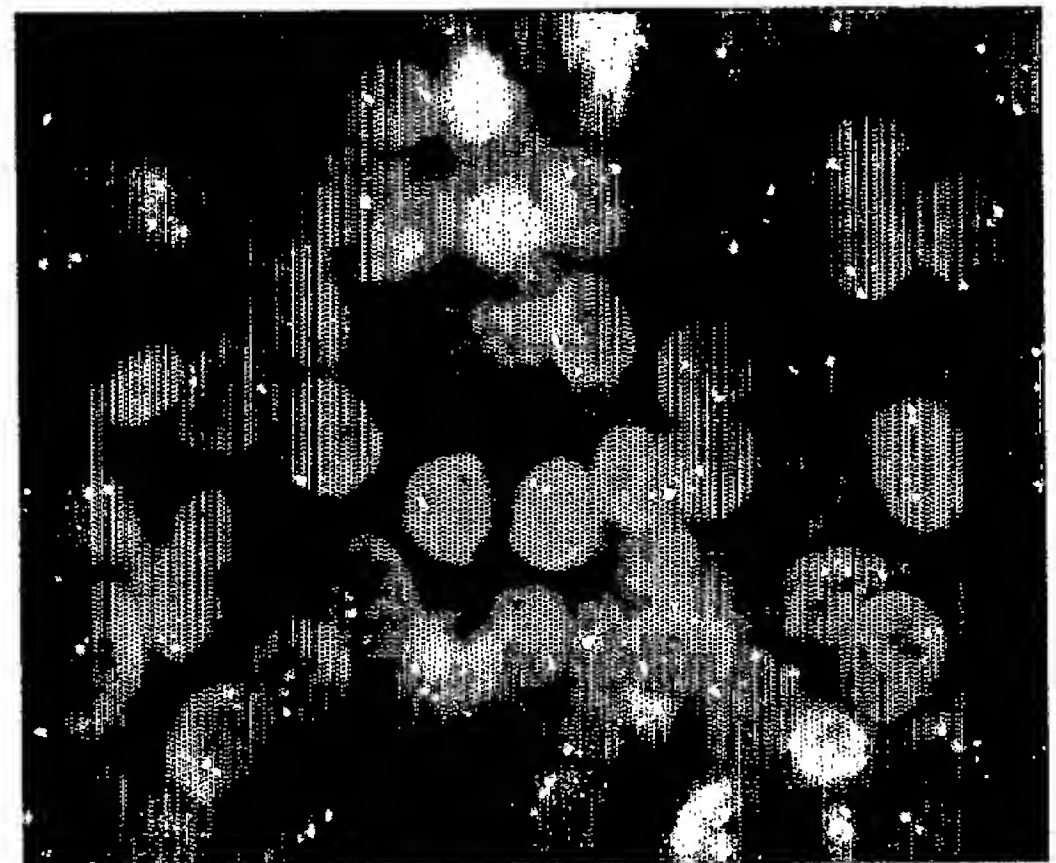


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**A**

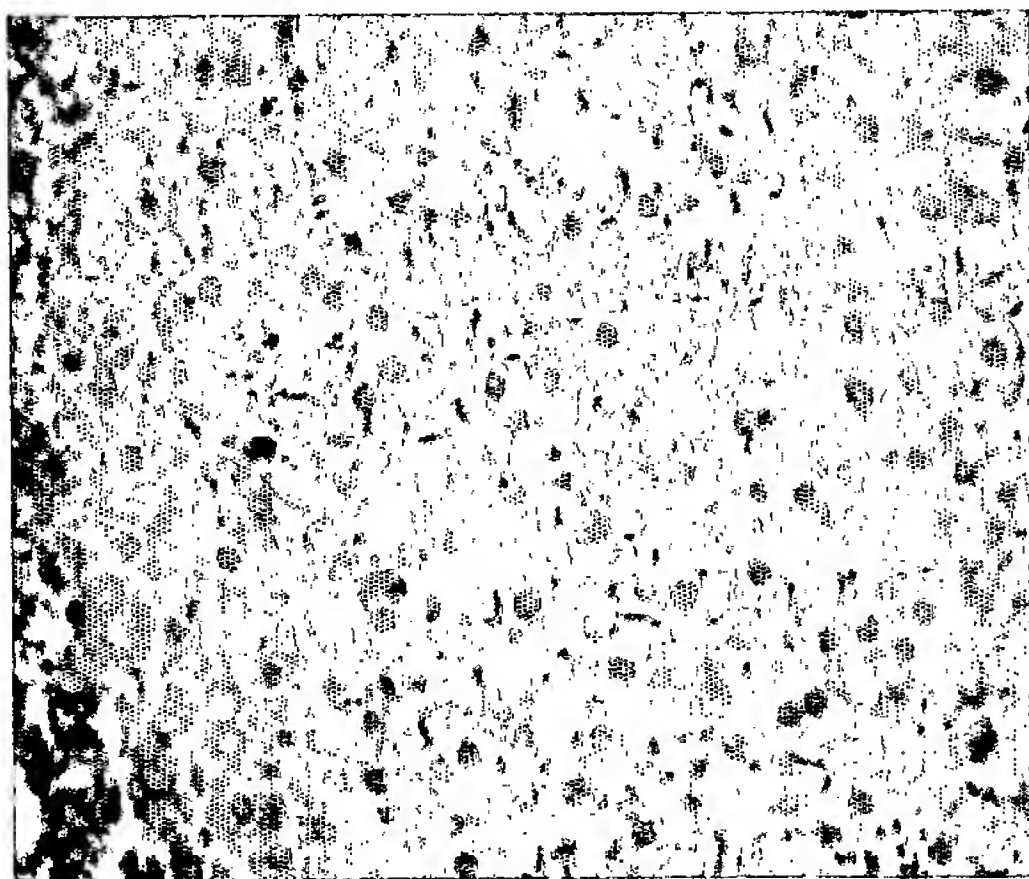


Normal and tumoral tissue

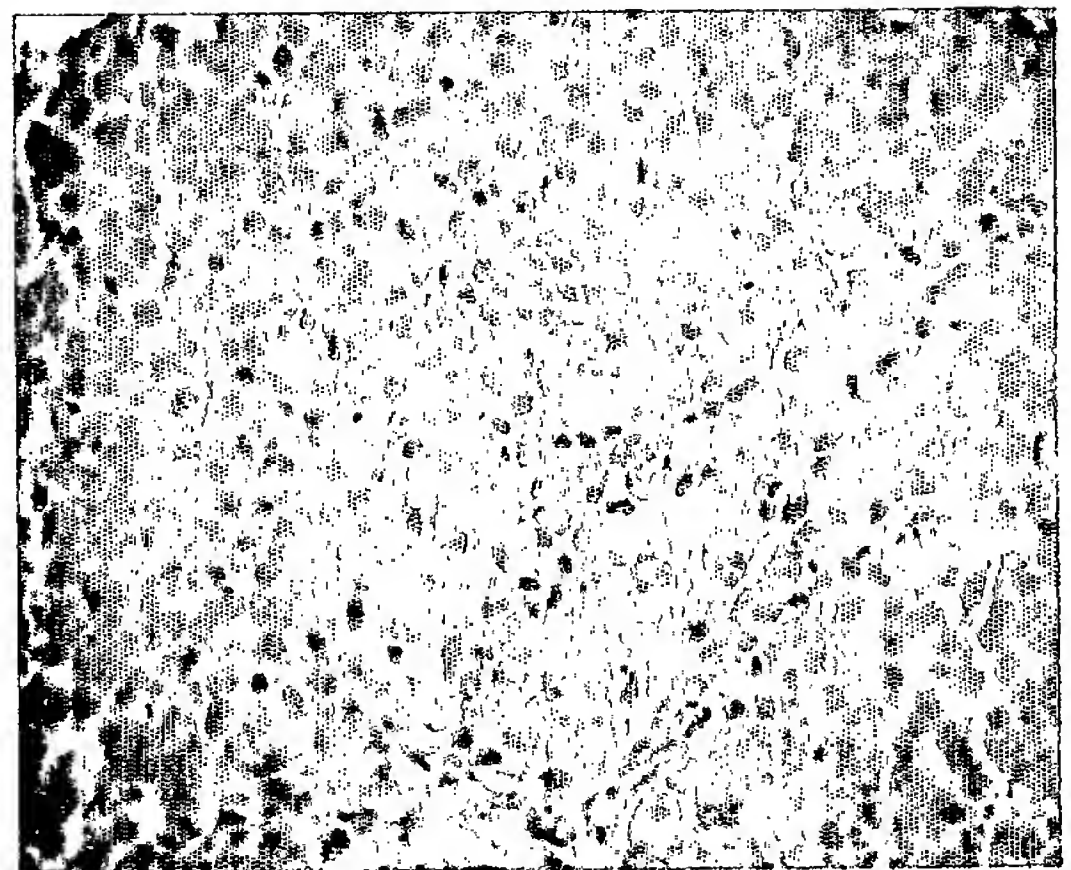


Tumoral tissue  
(not metastatic)

**B**



Normal tissue

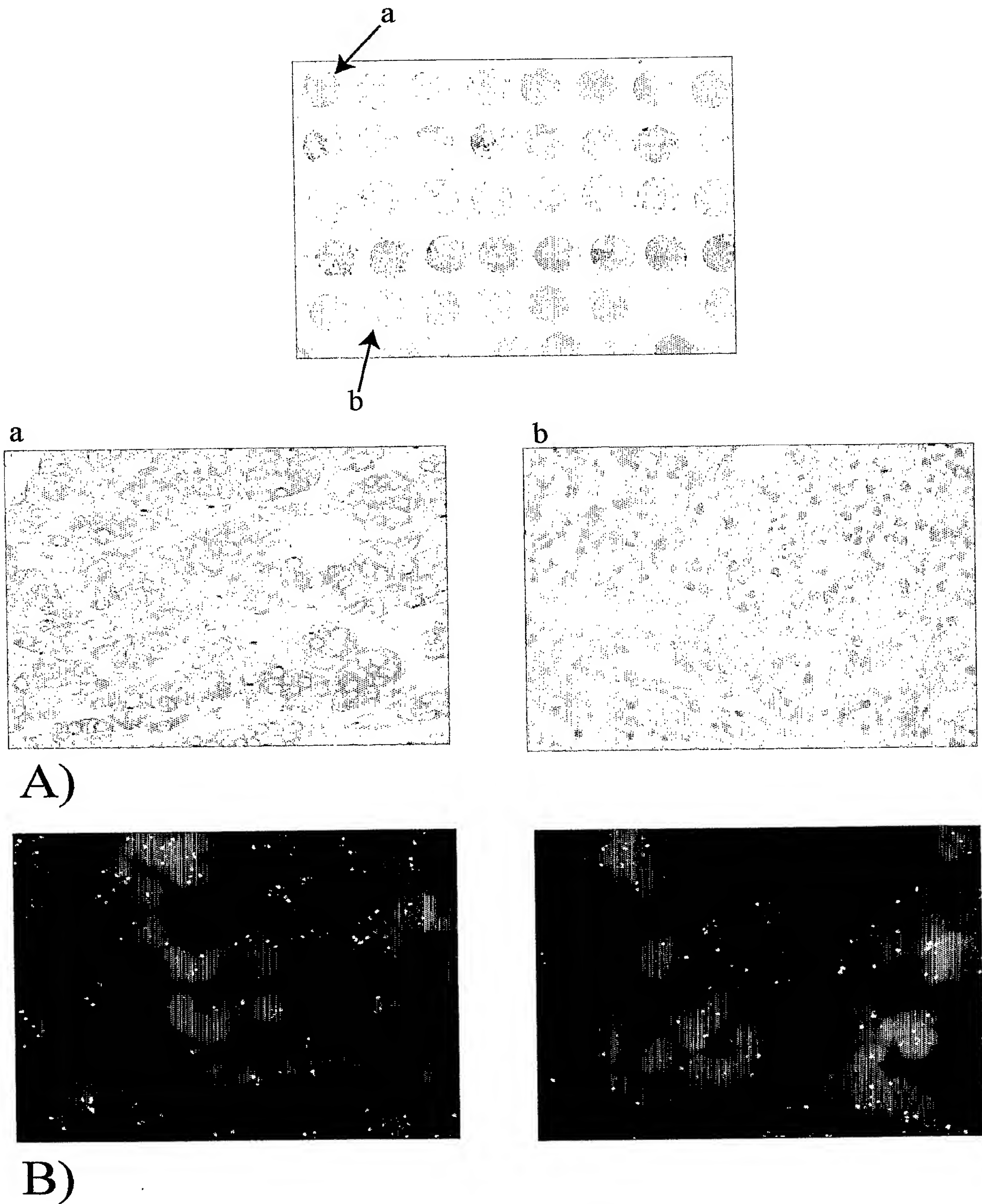


Tumoral tissue  
(not metastatic)

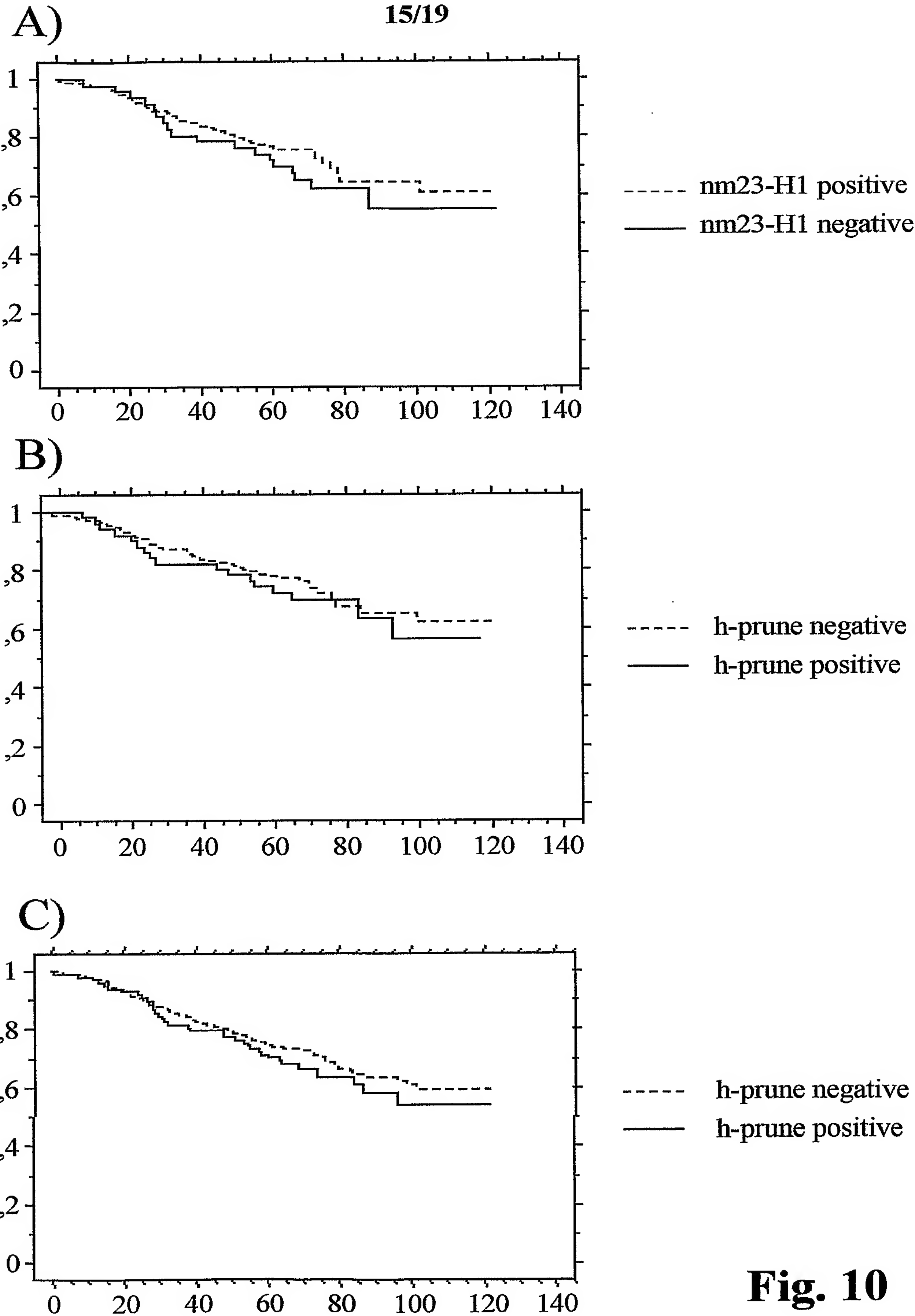
**Fig. 8**



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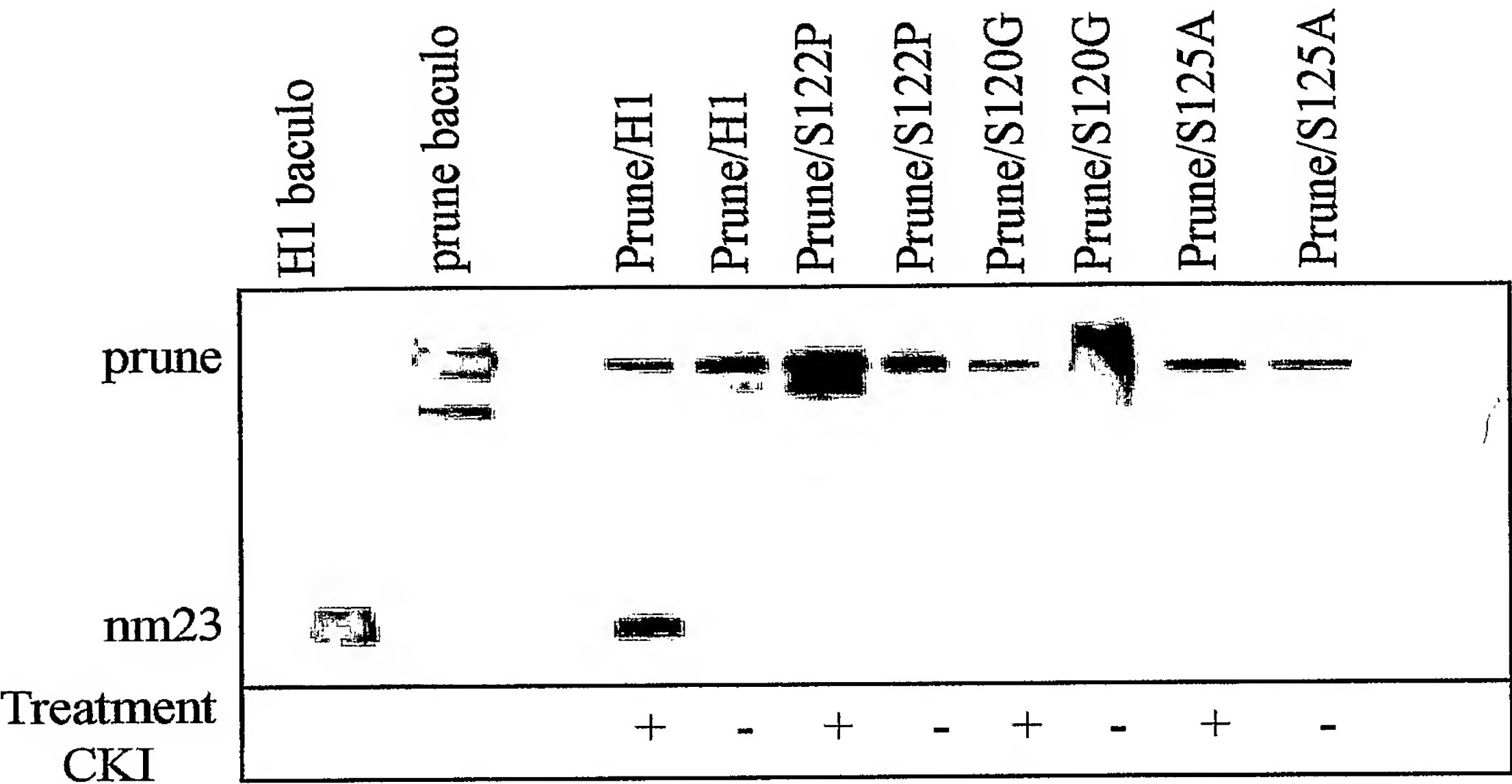


**Fig. 9**



**Fig. 10**

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A)

B)

MYDVPDYASLGSPVEMA  
NLERTFIAIKPDGVQRGLV  
GEIIKRFEQKGFRLVAMK  
FLRASEEHLKQHYIDLKD  
RPFFPGLVKYMNSGPVVA  
MVWEGLNVVKTGRVML  
GETNPADSKPGTIRGDFCI  
QVGRNIIHGSDSVKSAEK  
EISLWFKPEELVDYKSCA  
HDWVYE

Fig. 11

Voyager Spec #1 MC[BP = 1344,6 21449]

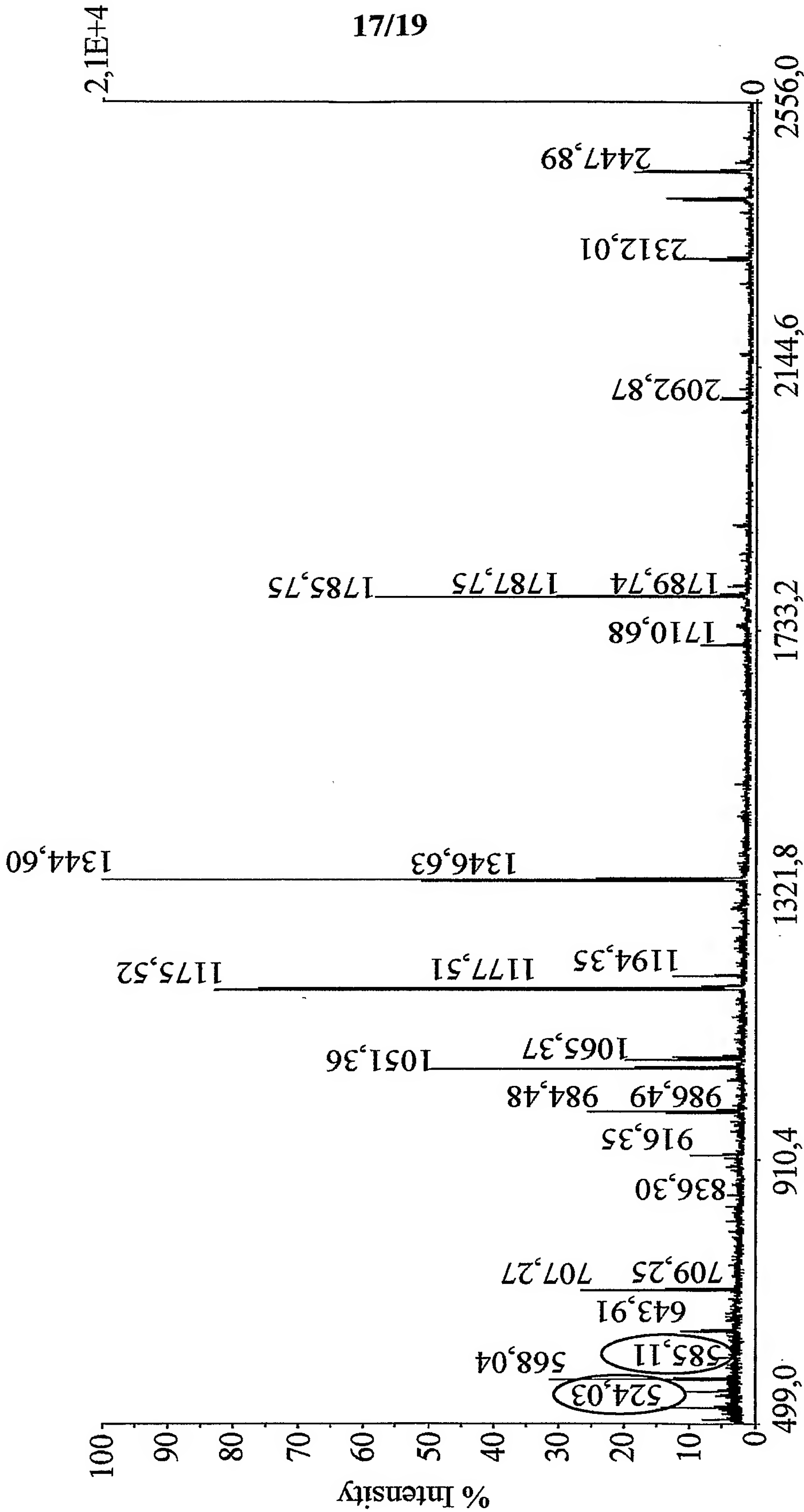


Fig. 11 C



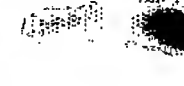









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A

	1	2	3	4
CKIδ	+	+	-	-
Isoform Nm23	H1	H2	H1	H2


nm23 → 

B

IC261	0h	2h	4h	6h	8h	0h
CIP	—	—	—	—	—	+
Phosphorecated nm23H1						
Total nm23H1						

C

	1	2	3	4	5
IC261 μMol		50	200	—	

h-prune → 

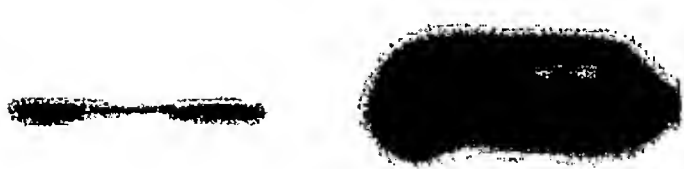
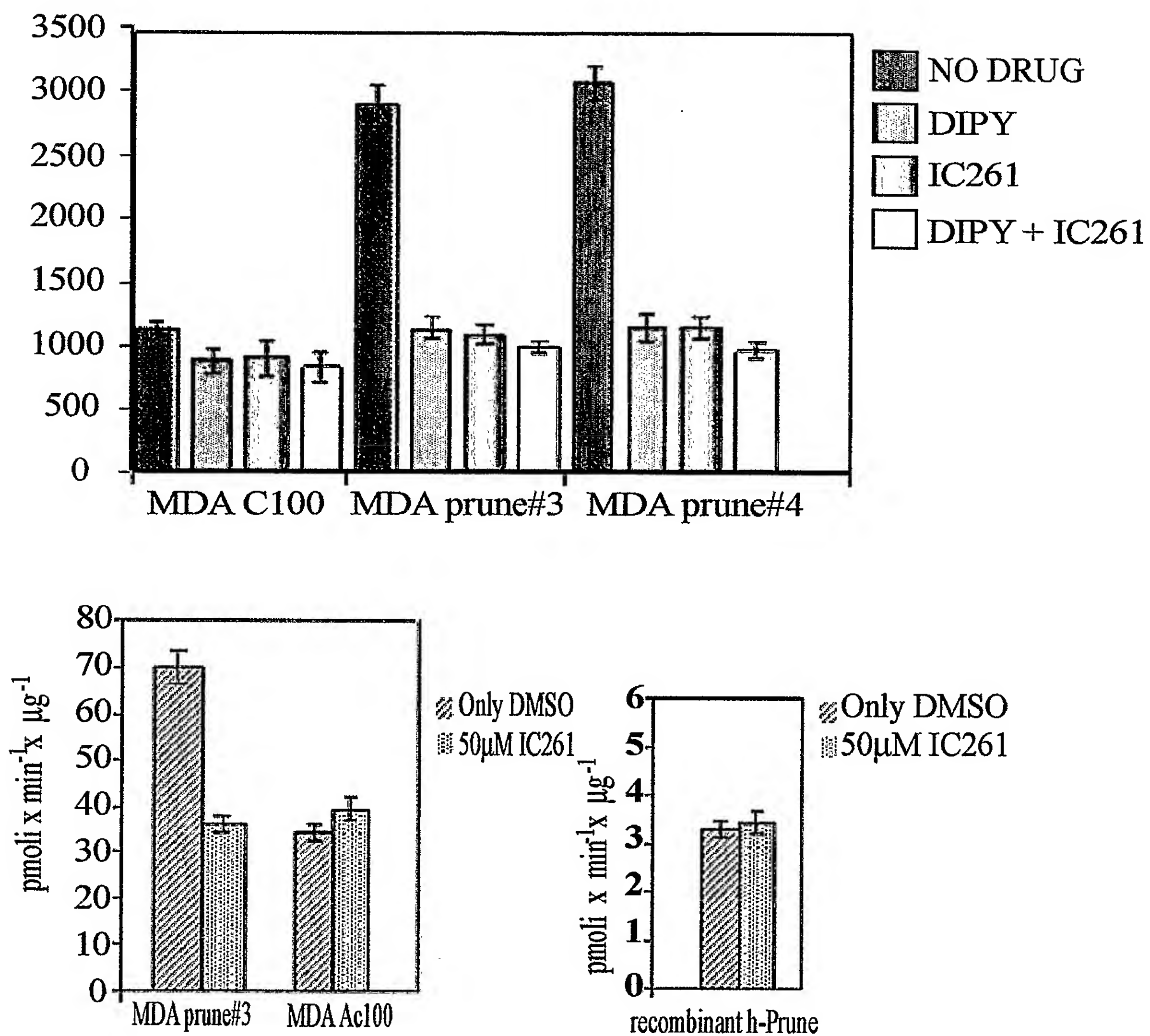
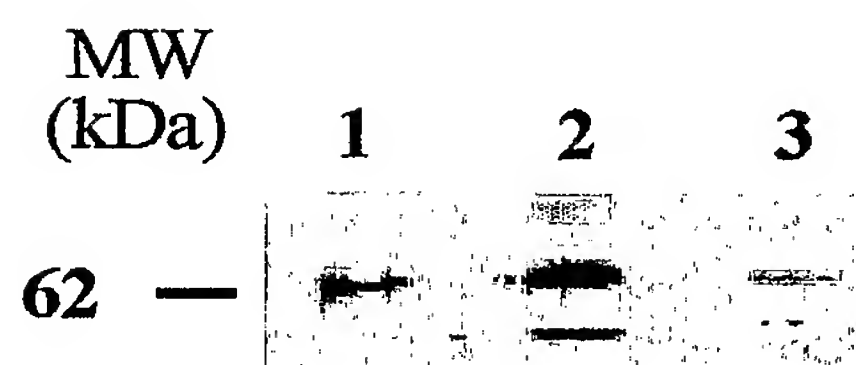
nm23H1 → 

Fig. 12



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**Fig. 13****Fig. 14**